ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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The Relationship Between the Acid Pocket and GERD

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G&H How was the acid pocket first discovered?

GB The acid pocket was first reported in 2001 by Fletcher and colleagues in an article published in *Gastroenterology*. The authors had observed that the pH of the esophagus was occasionally lower (ie, more acidic) than that of the stomach and wondered how this was possible. Therefore, they conducted a study in which a pH catheter was placed into the stomach of dyspeptic patients following a meal. The authors noted that, as the catheter was gradually pulled back, the pH measured 4 or 5 in the stomach, fell to approximately 2 in an area just below the sphincter of the esophagus, and then rose up to 6 or 7 in the esophagus. The region just below the esophageal sphincter, which was more acidic than the rest of the esophagus and stomach, seemed almost like a pocket of acid floating on top of the ingested meal. This pocket likely explained why the distal esophagus was sometimes more acidic than the stomach.

G&H How long after eating does this pocket of acid start to accumulate?

GB The pocket occurs quite rapidly. After 10 to 15 minutes, the stomach has secreted enough acid that the acid pocket starts to accumulate.

G&H What, specifically, causes this acid pocket?

GB The acid pocket is a physiologic phenomenon that occurs in all individuals, not just those with gastroesophageal reflux disease (GERD); thus, there is nothing abnormal about having an acid pocket. It is probably caused by gastric acid that does not mix properly with food and, as such, floats on top of ingested food. This discovery was initially surprising because gastric acid is supposed to mix with food to help with digestion.

In patients with GERD, gastric acid floats, or refluxes, back from the stomach or the pocket into the esophagus more often than in healthy individuals. It is unclear why this happens. A possible explanation is that patients with GERD commonly have a hiatal hernia, which means that the stomach (and thus the junction of the esophagus and the stomach) is positioned further into the thoracic cavity, placing the acid pocket inside the thoracic cavity as well, above the diaphragm. As a result, the protective effect of the diaphragm against reflux is lost, leading to a larger risk of the acid refluxing into the esophagus when the sphincter opens.

G&H How can the acid pocket be visualized?

GB Several methods can be used to visualize this phenomenon. In the method used in the study by Fletcher and colleagues, a pH catheter was placed into the stomach of the subjects and then slowly pulled back to note changes in pH, which allowed the authors to identify the upper and lower borders of the area with acid floating on top of the ingested meal.

My colleagues and I usually use the radiolabeled gastric acid method to visualize the acid pocket. A radiolabeled marker is infused into the blood circulation of an individual and then secreted by the cells producing gastric acid, thus enabling visualization of gastric acid secretion (including the location of the gastric acid in the stomach and the formation of a radiolabeled acid layer on top of the ingested meal). With this method, the acid pocket can easily be seen floating just below the esophageal sphincter.

The third method for visualizing the acid pocket involves magnetic resonance imaging. This radiologic method enables solid contents (ie, the ingested meal) to be differentiated from gastric contents (ie, gastric acid) based upon differences in density.

G&H Is the acid pocket associated with any conditions other than GERD?

GB Currently, there is no scientific evidence confirming a relationship between the acid pocket and other disorders. The acid pocket, which is very acidic, normally sits on top of the ingested meal, separated from the esophageal mucosa. If the pocket is close to the mucosa—or close to the sphincter, which separates the stomach and the esophagus—it may be possible that the acid pocket could contribute to an increased risk of dysplasia and even carcinoma; however, this is purely speculation and an issue that requires further evaluation.

G&H What effect do proton pump inhibitors have on the acid pocket?

GB Proton pump inhibitors cause the acid pocket to become a little smaller in volume and, more importantly, alter the composition of the pocket by increasing its pH (and, thus, decreasing its acidity). Normally, the acid pocket has a pH of approximately 2; after treatment with a proton pump inhibitor, the pocket's pH usually increases to 4 or 5. Thus, the pocket becomes less fortified and caustic.

G&H What agents have been used to disrupt or displace the acid pocket?

GB My colleagues and I have examined the prokinetic and macrolide agent azithromycin in an attempt to change the position of the acid pocket. Because prokinetic agents such as motilides increase the tone of the proximal stomach, it was thought that azithromycin might be able to push the acid pocket more distally, which would decrease the risk of acid reflux. Thus, we conducted a study in patients with small and large hiatal hernias and found that azithromycin did indeed change the position of the acid pocket but only in patients with small (<3 cm) hiatal hernias. In patients with large hiatal hernias, the acid pockets were too dislocated to induce any change with this therapeutic approach. Since these findings are not spectacular, this is clearly not the solution for managing GERD symptoms; however, these findings do illustrate that manipulating the position of the acid pocket may alter the risk of acid reflux.

Another potential therapeutic approach is to capture the acid pocket by making it react with a chemical compound such as an alginate. This substance makes a viscous solution when it comes into contact with acid; thus, when an alginate interacts with the acid pocket, it forms a foam that floats (or colocalizes), creating a "raft" that acts as a physical barrier and neutralizes the pocket. In a study recently published in *Clinical Gastroenterology and Hepatology*, my colleagues and I showed that, by labeling the acid pocket and the alginate, colocalization can clearly be seen in the upper stomach. We found that the number of acid reflux episodes could be reduced by administering an alginate. Thus, this is another way of specifically targeting the acid pocket in the hope of reducing the risk of acid refluxing back into the esophagus. Unfortunately, this agent has only been examined in a small number of patients and needs to undergo further research.

G&H What are the next steps in research in this area?

GB The next step should be to determine whether interactions between the acid pocket and the alginate compound, for example, can improve our approach to treating patients with GERD (though, most likely, only those with mild GERD). In my opinion, it may be most useful to determine whether interaction with the acid pocket may improve symptom control in patients who are still symptomatic despite receiving treatment with proton pump inhibitors. It is known that alginates are commonly used over-the-counter by many individuals and are effective, but the main challenge will be to study whether adding an alginate or another agent that targets the acid pocket may improve the suppression of reflux symptoms in partial responders to proton pump inhibitors.

Dr Boeckxstaens is a speaker and consultant for Reckitt Benckiser.

Suggested Reading

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